IJPSR (2012), Vol. 3, Issue 12 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 20 August, 2012; received in revised form 29 October, 2012; accepted 25 November, 2012

A STUDY OF AQUEOUS FILM COATING ON MICROCRYSTALLINE HYDROXY APATITE COMPLEX TABLETS

N. Narayanan*[1], S. Daisy Chella Kumari [1], N. Deattu [2] and V. Revathi [3]

Department of Pharmaceutics, College of Pharmacy, Madras Medical College [1], Chennai, Tamil Nadu, India
Sri Ramachandra College of Pharmacy, SRMC University [2], Porur, Chennai, Tamil Nadu, India
Department of Pharmaceutics, Sri Ramachandra College of Pharmacy [3], SRMC University, Porur, Chennai, Tamil Nadu, India

Keywords:
Microcrystalline Hydroxy Apatite Complex, Film coating of tablets, Hydroxy propyl methyl cellulose, Poly vinyl pyrrolidone

Correspondence to Author:

Dr. N. Narayanan

Director, Department of Pharmaceutics, College of Pharmacy, Madras Medical College, Chennai, Tamil Nadu, India

QUICK RESPONSE CODE

IJPSR:
ICV (2011)- 5.07

Website:
www.ijpsr.com

ABSTRACT

Water soluble polymers such as Hydroxy Propyl Methyl Cellulose (HPMC), Poly Vinyl Pyrrolidone (PVP), Carboxy Methyl Cellulose - Sodium (CMC - Na), and Methyl Cellulose as well as in combination of varying proportions are used in this study for the protective coating of Microcrystalline Hydroxy Apatite Complex (MCHC). The objective of this study was to investigate the effect of aqueous film coating on MCHC tablets evaluated by comparison with plain MCHC tablets and non-aqueous coated tablets. The parameters evaluated were the film smoothness, shininess, coating uniformity, percentage weight increase, hardness, disintegration time, dissolution study, moisture adsorption, stability and toxicity. An aqueous film coating solution in different combinations was applied on the tablets using a laboratory coating pan at 60^{o}C, in the atmospheric pressure. By using the same method non aqueous film coating solution was applied on the MCHC tablets and the tablet bed temperature maintained at 40^{o}C. The study has shown that HPMC and PVP combination in the proportion of 5% and 1% as coating material gave promising results in the evaluation of tablets.

INTRODUCTION: Drug particles or tablets, which are sensitive to moisture degradation, may be protected against moisture uptake through film coating[1]. The aqueous based system as coating material for solid dosage form has been gaining popularity owing to the fact, the organic based system presently followed are costly and also considered hazardous to health, safety and environment.

The film coat must as a matter of necessity to dissolve or rupture after ingestion of the tablet in order not to impair disintegration and dissolution of the tablets. Consequently only water soluble or water swellable polymers are suitable candidates for such coating solutions. The important objective of this study is coating of dosage form is a necessary aspect in the manufacture of drug products to increase the elegance and to impart protection to the drug. This work introduces a new step in the coating process. Microcrystalline Hydroxy Apatite Complex (MCHC), a drug of natural origin was chosen as the experimental drug, which itself has a protein matrix, which promotes bone metabolism. The MCHC supplies the body both the inorganic and organic components of bone tissue in their natural proportions [2]. The inorganic fraction consists of calcium, phosphorus, fluorine and trace elements [3]. The organic matrix ossein consists mainly of collagen, amino acids and proteoglycon [4].

In the present study, the emphasis was laid on the suitability of the different combinations of aqueous based polymers as coating material for MCHC tablets and they were evaluated and compared with non aqueous coated tablets for various parameters.

MATERIALS AND METHODS: Microcrystalline Hydroxy Apatite Complex and Hydroxy Propyl Methyl Cellulose (HPMC USP, 15 cps – Pharmacoat 615–Shin Etsu Chemical Co. Tokyo, Japan), Poly Vinyl Pyrrolidone (PVP – K 29/32 USP-GAF Chemicals Corporation, Great Britain), Carboxy Methyl Cellulose Sodium (CMC-Na BPC- Danicel Chemicals, Japan), Methyl Cellulose (MC USP, 15 cps - Methocel A 15 LV premium - Dow Chemical Co. Tokyo, Japan). Other materials used in the study like aerosil, starch, gelatin and gum acacia were of analytical grade and procured from commercial sources.

1. **Preparation of Microcrystalline Hydroxy Apatite Complex Tablets:** Microcrystalline Hydroxy Apatite Complex, starch and gum acacia were mixed thoroughly. Starch, gelatin and gum acacia are used as tablet binder. Gelatin was soaked in water and added to starch mucilage, heated till a smooth paste was formed. The dry mix was mixed with the paste and the wet material was transferred to a fluidized bed dryer at 60-70^{o}C for 20 min. Then passed through the mesh 14 and dried at 60-70^{o}C for 40 min. The dry granules were mixed with magnesium stearate as a lubricant, talc and aerosil as glidants. Aerosil (Degussa) chemically silicon dioxide is hygroscopic, used in aqueous system at a pH of 0-7.5 [5]. It is effective in increasing the viscosity of a system and because of its hydro phobic surface that greatly minimize their hygro scopicity. The granules were filled in the 9 mm deep concave punches in the tablet punching machine and punched into tablets.

2. **Preparation of Aqueous Film Coating solution:** The weighed quantity of polymer was dispersed in 10% of Isopropyl alcohol (IPA). Poly Ethylene Glycol (PEG) 6000, PEG 200 and preservatives were dissolved in a portion of water and mixed with the polymer dispersion with constant stirring. Titanium dioxide and sunset yellow colour were uniformly suspended in the polymer dispersion.

3. **Preparation of Non-aqueous Film Coating Solution:** HPMC and PVP were dispersed in half of the IPA- ethylene chloride blend by using mechanical stirrer [6]. The plasticizers diethyl phthalate, castor oil and opacifier titanium dioxide, colouring agent opadry brown and preservatives were added to the polymeric dispersion.

4. **Coating Technique:** For each batch, 2 kg of MCHC tablets were coated at a time in a 5 kg capacity coating pan (Manesty Machines Ltd UK model 15096-8 14" size and 32 rpm) maintained at 60˚C and usual atmospheric pressure. For preliminary coating, 100 ml of aqueous polymeric dispersion was first sprayed on MCHC tablets, dried for 15 to 20 min at 60˚C to obtain the precoat [7]. This was followed by three applications of 100 ml each. In the aqueous polymeric dispersion, allowing 5 to 10 min drying interval between each application and drying is carried out finally for 30 min.

5. **Drug content:** The drug content in the coated MCHC tablets was determined for Calcium[8] and Phosphorus [9].

6. **Film Smoothness and shiningness:** The Physical appearance of the formulations, plain MCHC tablets, aqueous coated tablets and non-aqueous coated MCHC tablets were studied.

7. **Coating uniformity and Percentage weight increase:** All the batches were studied for coating uniformity by measuring the diameter and thickness of the coat by using 'Mitutoyo' Vernier Caliper. Weight increase is the difference between the weight of the coated tablet and the weight of the core tablet [10].

8. **Hardness:** The formulations were assessed for hardness using Monsanto tablet hardness tester.

9. **Disintegration Test:** Disintegration test was carried out in distilled water at 37±2^{o}C for all the samples of plain MCHC tablets, aqueous coated tablet and non- aqueous coated MCHC tablets as per the USP XXII method [11].

10. **Dissolution Test:** The samples of plain MCHC tablets, selected batches of aqueous coated MCHC tablets and non- aqueous coated MCHC tablets were studied for dissolution test in the simulated gastric fluid without pepsin [12]. The samples were withdrawn at regular intervals of 5, 10, 15 and 30 min and analyzed for Calcium and Phosphorus content.

11. **Moisture adsorption:** 10 tablets each of plain, aqueous coated and non- aqueous coated MCHC tablets were dried to constant weight and placed in desiccators maintained at RH 66% and 90% using saturated solution of sodium nitrite and saturated solution of zinc sulphate respectively [13]. The tablets were weighed after every 24 h for 5 days and the amount of moisture adsorbed was calculated [14].

12. **Stability Studies:** The physical stability of selected samples was performed by exposing the samples at 45˚C and at RH 85% in order to elucidate the influence of temperature and moisture on the parameters like appearance, hardness and disintegration time [15]. The samples were analyzed after 15 and 30 days.

13. **Toxicity Studies:** Toxicity studies were performed in *Swiss albino mice* on two best combinations selected (CH and CHP) among the formulations prepared . The samples were tested in the dose level of 5, 10 and 20 times of the human therapeutic dose (30 mg/kg body weight) and observed for their toxic effects [16]. The animals, *Swiss albino* mice, each weighing approximately 25 g were divided into four groups of 10 animals each, of which group II, III and IV were divided into two batches. Group I was treated as control and were treated with the coated tablets in suspension form by oral route and the results were recorded.

RESULTS AND DISCUSSION: One of the major steps in formulation development activity is bringing a stabilized film coating formulation. The aqueous based system in the coating of tablets has been gaining popularity owing to the advantages of safe handling and no environmental hazardous effect.

The organic based systems have solvents like Methylene chloride, Ethyl acetate, Acetone, Isopropyl alcohol etc., are costlier and also have health and environmental hazardous effect. In this context, a bold attempt was made on aqueous film coating of MCHC tablets using different polymers like Methyl cellulose (MC), Carboxy methyl cellulose sodium (CMC-Na), Polyvinyl pyrrolidone (PVP) and Hydroxy propyl methyl cellulose (HPMC) were evaluated and compared with plain MCHC tablets and non- aqueous coated tablets for various parameters.

The Microcrystalline Hydroxy Apatite Complex tablets were coated with 7 different batches of coating materials prepared with various coating agents (**Table 1**). The characteristics and assay of MCHC tablets were studied and tabulated (**Table 2**).

TABLE 1: PREPARATION OF AQUEOUS FILM COATING SOLUTION

S. No.	Ingredients	Batches (Quantity in %)						
		CM	CC	CP	CH	CHP	CHC	CHM
1.	Methyl Cellulose	1.0	-	-	-	-	-	0.5
2.	Carboxy Methyl Cellulose Sodium	-	1.0	-	-	-	0.5	-
3.	Poly Vinyl Pyrrolidone	-	-	5.0	-	1.0	-	-
4.	Hydroxy propyl Methyl Cellulose	-	-	-	6.0	5.0	5.0	5.0
5.	PEG 6000	0.4	2.0	2.0	2.0	2.0	2.0	0.4
6.	PEG 200	2.0	0.4	0.4	0.4	0.4	0.4	2.0
7.	Titanium dioxide	2.4	2.4	2.4	2.4	2.4	2.4	2.4
8.	Sunset Yellow	0.4	0.4	0.4	0.4	0.4	0.4	0.4
9.	Methyl paraben: Propyl paraben (2:1)	0.04	0.04	0.04	0.04	0.04	0.04	0.04
10.	Water	100	100	100	100	100	100	100

CM- Methyl Cellulose (MC); CC- Carboxymethyl Cellulose Sodium (CMC-Na); CP - Povidone (PVP); CH- Hydroxypropyl Methyl Cellulose (HPMC); CHP- HPMC and PVP (5% and 1%); CHC- HPMC and Na-CMC (5% and 1%); CHM- HPMC and Na-CMC (5% and 1%)

In the studies conducted for film smoothness and shiningness, different proportions of HPMC and PVP combinations respectively in percentage of 5 & 1, 5 & 2, 5 & 3, 5 & 4, 4 & 5, 3 & 5, 2 & 5 are used as coating material. In the studies conducted for film smoothness and shiningness the HPMC and PVP combination (5% and 1%) as coating material has proven to be superior to other combinations. The comparison of diameter and thickness of both aqueous and non-aqueous coated MCHC tablet with the plain tablets appeared uniform ranging from 9.08 mm to 9.13 mm in diameter and thickness from 4.15 mm to 4.22 mm. revealed that there was marginal increase in diameter and thickness of the coated tablets.

It was found that in aqueous based coating, percent weight increase was between 2.17 and 2.84 and in respect of non-aqueous based coating it is the lowest 1.84. It was observed that there was proportionate increase in the hardness with the increase in percent weight for all the formulations. The disintegration time for plain tablet was 10.17 min and for coated tablets 11.55 min, 10.45 min, 11.21 min, 10.47 min, 11.21 min, 10.45 min, 11.42 min all nearer to the value of the plain uncoated tablet (**Table 3**).

TABLE 2: CHARACTERIZATION OF MICROCRYSTALLINE HYDROXY APATITE COMPLEX TABLETS

S. No.	Parameters	Result	%
1	Diameter	9.05 mm	-
2	Thickness	4.07 mm	-
3	Hardness	5.0 kg	-
4	Disintegration	10 m	-
5	Dissolution (20 min.)	-	-
	Calcium	36.16 mg	109.57
	Phosphorous	15.36 mg	102.40

TABLE 3: EVALUATION OF AQUEOUS COATED MICROCRYSTALLINE HYDROXY APATITE COMPLEX TABLETS

S. No.	Batch	Diameter* (mm)	Thickness* (mm)	Tablet Weight (mg)	Weight increase (%)	Hardness (kg/cm^2)	Disintegration time	
							m	sec.
1.	**MCHC-P**	9.05	4.07**	299.50	-	5.0	10	17
2.	**CM**	9.12	4.17	307.00	2.50	6.0	11	55
3.	**CC**	9.12	4.21	307.00	2.50	6.0	10	45
4.	**CP**	9.09	4.16	306.00	2.17	5.5	11	21
5.	**CH**	9.11	4.18	307.00	2.50	6.5	10	47
6.	**CHP**	9.11	4.19	308.00	2.84	7.0	11	21
7.	**CHC**	9.13	4.22	307.00	2.50	6.0	10	45
8.	**CHM**	9.13	4.20	306.00	2.17	5.5	11	42
9.	**MCHC-N**	9.08	4.08	305.00	1.84	7.0	12	57

* Average of 10 readings; ** Uncoated MCHC tablets; MCHC-P- Microcrystalline Hydroxy Apatite Complex core Tablet; MCHC-N- Microcrystalline Hydroxy Apatite Complex Tablets coated with polymers in non- aqueous solvents

The results obtained gave no significant indications as to the influence of the aqueous polymer on the disintegration time of the coated tablets. However there was marginal increase in the disintegration time for non-aqueous coated MCHC tablets, the reason attributable to the poor permeability of the film to the water.

The results of dissolution test indicated that the percentage of calcium and phosphorus release was found to be 102.99, 103.3 for plain tablets, 98.41, 104.2 for the HPMC- aqueous coated tablets, 101.01, 103.0 for the HPMC- PVP combined aqueous coated tablets and 98.41 and 105.1 for the HPMC - PVP combined non aqueous coated tablets at 20 min. (**Table 4 and Fig. 1**).

In dissolution study, at 20 min. all the results are nearer to the standard value i.e. 33 mg and 15 mg of calcium and phosphorus respectively in MCHC tablets. Moisture adsorption studies of tablets revealed that the plain tablets of MCHC adsorbed the moisture at a slightly faster rate than the aqueous and non-aqueous coated tablets.

Equilibrium achieved in 96 h was evident for the constant moisture content of tablets. Povidone alone as coating material showed a faster rate of moisture adsorption (12.52% at RH 90%) compared to povidone in combination with HPMC as coating material. The Physical stability studies of the coated tablet showed that no remarkable changes in the hardness and the disintegration time after 15 and 30 days, which revealed the fact that the HPMC and PVP combination acted as safe aqueous coating material.

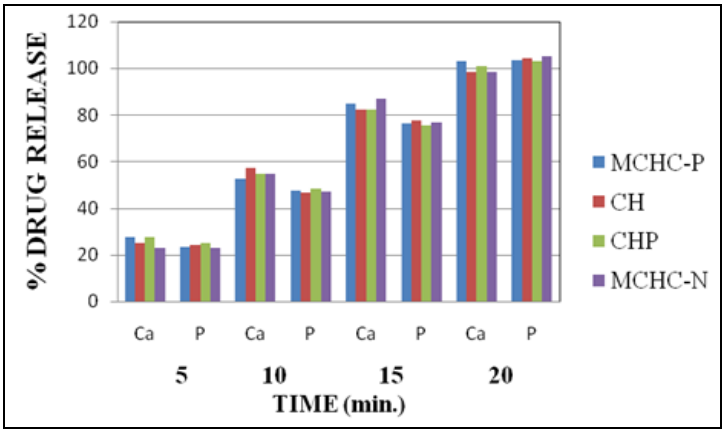

FIG. 1: DISSOLUTION PROFILE OF PLAIN, SELECTED AQUEOUS NON- AQUEOUS COATED TABLET IN THE MEDIUM OF pH 1.2±0.1
(Ca – Calcium; P - Phosphorous)

Toxicity studies conducted in *Swiss albino* mice on the best two samples selected namely HPMC (6%) coated tablets and HPMC and PVP (5% and 1%) coated tablets indicated no noticeable untoward effects in the experimental animals (**Table 5**).

TABLE 4: DISSOLUTION PROFILE OF PLAIN, AQUEOUS COATED AND NON-AQUEOUS MCHC TABLETS

S. No.	Batch	Drug Release in %											
		5		10		15		20		25		30	
		Ca	P	Ca	P	Ca	P	Ca	P	Ca	P	Ca	P
1	**MCHC-P**	27.6	23.5	52.6	47.53	84.68	76.20	102.99	103.3	102.4	101.5	102.2	102.4
2	**CH**	25.2	24.3	57.2	46.73	82.39	77.46	98.41	104.2	99.35	103.4	99.54	102.3
3	**CHP**	27.6	25.1	54.9	48.26	82.39	75.46	101.01	103.0	101.3	103.5	100.8	103.2
4	**MCHC-N**	23.0	22.7	54.9	47.06	86.97	76.66	98.41	105.1	99.18	104.5	100.9	104.4

TABLE 5: TOXICITY STUDY OF AQUEOUS COATED MCHC TABLETS

Group	Treatment	Dose (mg)			Toxicity	
		MCHC-P	CH	CHP	24 h	48 h
I (Control)	20 times the human dose	15.0	-	-	Nil	Nil
II	5 times the human dose	-	3.75	3.75	Nil	Nil
III	10 times the human dose	-	7.50	7.50	Nil	Nil
IV	20 times the human dose	-	15.0	15.0	Nil	Nil

CONCLUSION: This methodology provides a safe, reproducible and easy method of production of aqueous film coated tablets. An added advantage of this methodology is its cost effectiveness and also the resultant products are smooth with extra shiningness. The study has given a formulation approach for adopting aqueous soluble polymers in combination of HPMC and PVP 5 and 1 % respectively to assess its suitability as good coating material than all batches of the present work..

ACKNOWLEDGEMENT: The authors wish to thank Dr. M.S.R. Moorthi, Former R&D Chief, TTK Pharma, Pallavaram, Chennai – 44, and Prof. A.V. Ramanathan, Retired Prof. of Pharmaceutics, Madurai Medical College, Madurai – 20.

REFERENCES:

1. Liberman HA, Lachman L , Schwartz JB . Pharmaceutical Dosage Forms: Tablets; Vol 1, Marcel Dekker: New York.1989; 81-127.
2. Epstein O, Kato Y, Dick R, Sherlock S. Vit D, Hydroxyapatite and Calcium Gluconate in the treatment of Cortical Bone thinning in post-menopausal women with Primary Biliary Cirrhosis. The American Journal of Clinical Nutrition. 1982; 33: 426-30.
3. Dent CE, Davies IJ. Calcium Metabolism in bone disease: Effects of treatment with microcrystalline calcium hydroxyl apatite compound and dihydrotacysterol. Journal of Royal Society of Medicine,, 1980; 73 (11): 780-82.
4. Nilson KH, Jayson MI, Dixon A. Microcrystalline Calcium hydroxyapatite Compound in Corticosteroid treated rheumatoid patients; a controlled study: British Medical Journal, 1978; 2:1124-26.
5. Raymond C Rowe, Paul J Sheskey, Marian E Quinn. Handbook of Pharmaceutical Excipients Fifth Edition, International Journal of Pharmaceutics. 2006. 188-191.
6. Arwidsson Hans, Barbo Johansson. Application of intrinsic viscosity and interaction constant as a formulation tool for film coating. III. Mechanical studies on free ethyl cellulose films, cast from organic solvents Fifth Edition, International Journal of Pharmaceutics. 1991; 56 (1-2): 91-97.
7. Mc Ginity JW. Pharmaceutical Dosage forms. Third Edition, Marcel Dekker, New York, 1988; 49-92.
8. Indian Pharmacopoeia. Volume 1, Ministry of Health and Family Welfare, Government of India, Controller of Publications, New Delhi: 1985; 84-85.
9. Garrat DC. The Quantitative Analysis of Drugs, Third Edition Chapman and Hall Ltd; London: 1964; 533 -537.
10. Philip W Stern. Effect of film coating on tablet hardness. Journal of Pharmaceutical Sciences. 1976; 1291-1295.
11. United States Pharmacopoeia. XXII Edition, U.S Pharmacopoeial convention Inc, Mac.Roctville, USA, 1990; 1577-1579.
12. United States Pharmacopoeia. XIX Edition, U.S Pharmacopoeial convention Inc, Mac Publishing Co. Easton, USA, 1975; 765.
13. Malamataris S, Karidas T, Goidas P. Effect of Particle size and sorbed moisture on the compression behavior of some Hydroxy Propyl Methyl Cellulose Polymers. International Journal of Pharmaceutics.1994; 103 (3): 205-215.
14. Perry RH, Green DW. Perry's Chemical Engineer's Handbook, Fourth edition, McGraw Hill Book Co; New York: 1997; 15-41.
15. Martin A, Swarbrick J and Cammarata A. Physical Pharmacy, Third Edition, B.I Waverly (P) Ltd; New Delhi: 1996; 391 - 395.
16. Ghosh MN. Fundamentals of Experimental Pharmacology, Scientific Books publication, Calcutta. 1971; 84 - 88.

How to cite this article:
Narayanan N, Kumari SDC, Deattu N and Revathi V: A Study of Aqueous Film Coating on Microcrystalline Hydroxy Apatite Complex Tablets. *Int J Pharm Sci Res*. 3(12); 4851-4855.